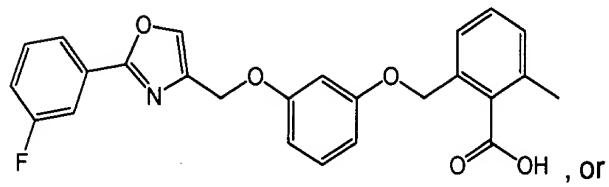
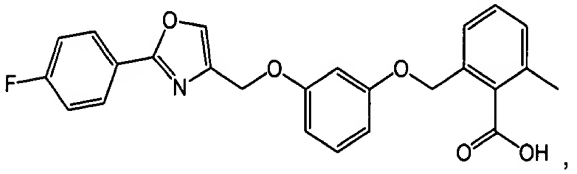
97. (New) A compound as claimed in claim 1, wherein the compound is

a11



, or



,

or a pharmaceutically acceptable salt, hydrate or solvate thereof.

Remarks

I. Subject matter withdrawn from consideration

In response to the non-Final Office Action, applicants raised a number of concerns about the election of species requirement and subject matter withdrawn from consideration. The Examiner did not respond to those concerns or even address them in the Final Office Action. Applicants therefore respectfully request that the Examiner address the comments presented below.

A. Scope of Ar I examined in the search

In the Office Action of September 20, 2002, the Examiner asked the applicants to elect a single disclosed species to begin examination. Applicants elected the compound of Example 7z on page 108 of the application. The elected compound has the structure shown in amended claim 94 and comprises a group Ar I as a heteroaryl group. Applicants have corrected the formula of claim 94 to properly recite the structure of the elected compound named in Example 7z on page 108 of the application. The heteroaryl group is a substituted oxazoyl group. The Examiner mentioned that the elected compound was not found in the search and that the search was expanded to compounds where Ar I is a fused arylheterocyclyl. The Examiner mentioned that prior art was found for this new subgenus. The document cited by the Examiner, U.S. Patent

No. 5,051,427, discloses compounds having a quinoline group in the position corresponding to Ar I of the invention. A quinoline group falls within the definition of "heteroaryl," not within the definition of "fused arylheterocyclyl." *See* specification at page 12, line 18. Applicants respectfully request confirmation that the full scope of "heteroaryl" for variable Ar I was examined and also request clarification as to what additional Ar I groups, if any, were examined.

B. Compound claims withdrawn from consideration

The Examiner withdrew compound claims 3-6, 8, 10-13, 16-19, 22, 24-26, 28-38, 40-48 and 90-93 from consideration as not reading on the elected species. Applicants disagree with that list of claims. Some of those claims do literally read on the elected species. On the other hand, some claims left in consideration by the Examiner do not literally read on the elected species.

Claims 11, 22, 31, 34-37, 91 and 93, which were withdrawn from consideration, do literally read on the elected species. New claims 95-97 also literally cover the elected species as a recited compound in each claim. Support for the new claims appears in original claims 39 and 40. Claims 9 and 39, which were apparently still being examined, do not literally read on the elected species.

The compound claims that do not literally read on the elected species, and which applicants assume the Examiner would withdraw from consideration, are therefore claims 3-6, 8-10, 12-13, 16-19, 24-26, 28-30, 32-33, 38-48, 90 and 92. Applicants have canceled those claims in this amendment, but reserve the right to pursue that canceled subject matter in a separate patent application.

The compound claims that do literally read on the elected species, and which should be examined, are claims 1-2, 7, 11, 14-15, 20-23, 27, 31, 34-37, 89, 91 and 93-97. Additional claims, including a composition claim and method claims, are discussed below.

C. Method claims and composition claim withdrawn from consideration

The Examiner withdrew claims 50-88 from consideration. Applicants do not agree that all those claims should be withdrawn from consideration. The Examiner

never required applicants to elect between compounds and methods of using compounds in any restriction requirement. Instead, the Examiner asked applicants to only elect a species to begin examination. Claims 50-65 and 67-82 literally read on the use of the elected species. Claims 83-88 do not. Claim 66 recites a pharmaceutical composition comprising a compound that covers the elected species. Applicants respectfully request that the Examiner include claims 50-82 for examination, as those claims do not constitute a "non-elected" invention.

II. Rejection under 35 U.S.C. § 102

The Examiner maintained the rejection of claims 1, 2, 7, 9, 14, 15, 20, 21, 23, 27, 39, 49 and 89 under 35 U.S.C. § 102(b) as anticipated by U.S. Patent No. 5,051,427 to Huang et al. ("Huang"). In support of the rejection, the Examiner argued that Huang anticipated the claims when variable "B" of the invention is defined as a bond and, simultaneously, variables c or d are a value greater than zero. Applicants have amended claims 1 and 27 to delete the definition of variable "B" as a chemical bond.

Huang discloses compounds of its own formula I that contain a group $-(C)_dR_1R_2-$, where d is 1-5, in the position corresponding to group "B" of the invention. That formula does not teach a group B as defined in amended claims 1 or 27, which is -O-, -S-, -SO-, $-SO_2-$, $-NR_{17}-$, ethynylene, -C(O)-, $-N(R_{18})C(O)-$, or $-C(O)NR_{18}-$. Huang does not suggest the claimed compounds from an obviousness perspective either. The document provides no motivation for replacing the carbon atom "C" with heteroatoms in a way needed to reach the compound of the invention or for otherwise modifying any aspect of its group $-(C)_dR_1R_2-$ to result in a compound of the invention.

III. Rejection under 35 U.S.C. § 112, second paragraph

The Examiner maintained the rejection of certain claims under 35 U.S.C. § 112, second paragraph, as indefinite. The Examiner argued that the terms "optionally substituted," "heterocyclyl" and "heteroarylalkyl" were indefinite, and that it was not sufficient to refer to their definitions in the specification. The original rejection involved claims 1, 2, 27 and 49. The Final Office Action states that the rejection applies now to claims 10, 11 and 13. Claims 10 and 13 have been canceled, and claim 11 does not

contain any of the disputed terms. Applicants respectfully request clarification on what claims are rejected.

Applicants amended claim 1 to define a number of terms used in the claim, including the terms "alkyl," "aryl," "heteroaryl," "heterocyclyl," "heteroaralky," "alkyl group substituent" and "ring system substituent." Support for those definitions appears on pages 7-15 of the specification in the section titled "Definitions." This amendment to add the definitions of the disputed terms in the claims themselves should be sufficient to more clearly define the invention and overcome the rejection.

Also in an effort to more clearly define the invention, applicants have amended the claims to define Ar I as a heteroaryl group and to define Ar II and Ar III as aryl groups. This amendment is consistent with the structure of the elected species. Claims 2, 20 and 21 were amended to reflect the revised definitions of the groups Ar I, Ar II and Ar III in claim 1. The definitions of R' and R" in claim 27 were amended to recite that the groups are hydrogen or ring system substituents. Support for reciting the groups as hydrogen appears in the original definition of "ring system substituents," which included hydrogen. Claims 22 and 89 have been amended to recite straight or branched lower alkyl groups. Claim 36 was amended to recite R" as an alkyl group. Claims 51, 58, 68, 75 and 91 have been amended to provide proper antecedent basis and to correct a grammatical error. Lastly, and as mentioned in the discussion of the restriction requirement, applicants have corrected the formula of claim 94 to properly recite the structure of the elected compound named in Example 7z on page 108 of the application.

In view of the above, the pending claims should be patentable over the cited art and should satisfy the requirements of 35 U.S.C. § 112, second paragraph. If there is any fee due in connection with the filing of this Amendment, please charge the fee to our Deposit Account No. 06-0916.

Respectfully submitted,

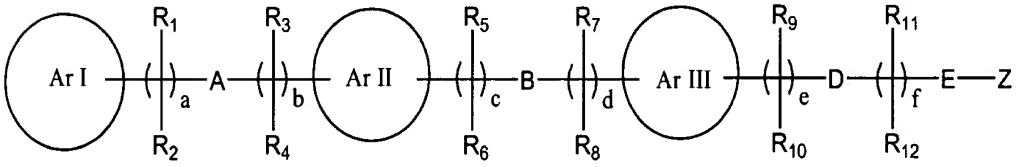
FINNEGAN, HENDERSON, FARABOW,
GARRETT & DUNNER, L.L.P.

By: _____
Steven J. Scott
Reg. No. 43,911
202 408-4000

Date: June 30, 2003

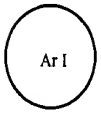
Appendix I Detailing Amendments to Claims

1. (Twice Amended) A compound of formula I

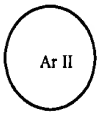


(I)

wherein:



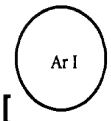
is heteroaryl, which is optionally substituted by one or more ring system substituents;



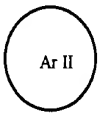
and

are, independently, aryl, which are optionally substituted by one or more ring system substituents;

[



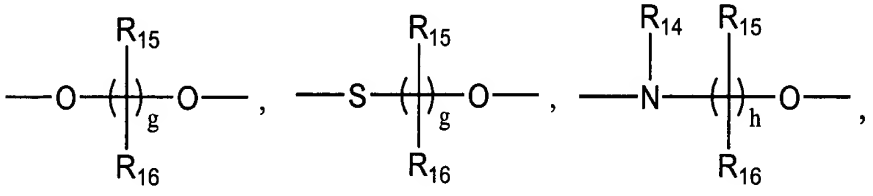
,



, and

are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;]

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



;

B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, [a chemical bond,] ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently -$(CH_2)_q$-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO_2-, -SR_{23}, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$-2,4-thiazolidinedionyl, or tetrazolyl; and

R_{21} is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

wherein

"alkyl" is an aliphatic hydrocarbon group which is straight or branched having 1 to about 20 carbon atoms and is optionally substituted by one or more alkyl group substituents;

"aryl" is an aromatic monocyclic or multicyclic ring system of about 6 to about 14 carbon atoms, which is optionally substituted by one or more ring system substituents;

"heteroaryl" is an aromatic monocyclic or multicyclic ring system of about 5 to about 14 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heterocyclyl" is a non-aromatic saturated monocyclic or multicyclic ring system of 3 to about 10 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

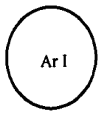
"heteroaralkyl" is a heteroaryl-alkyl group, wherein the heteroaryl and alkyl groups are as defined above;

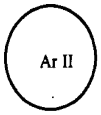
an "alkyl group substituent" is halo, carboxy, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aryl, alkoxy, alkoxycarbonyl, aralkoxycarbonyl, heteroaralkoxycarbonyl, or Y^1Y^2NCO-, wherein Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or Y^1 and Y^2 taken together with the nitrogen atom to which Y^1 and Y^2 are attached form heterocyclyl

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein; and

a "ring system substituent" is alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, fused cycloalkyl, fused cycloalkenyl, fused heterocyclyl, fused heterocyclenyl, arylazo, heteroarylazo, R^aR^bN-, R^cR^dNCO-, R^cO_2CN-, or $R^cR^dNSO_2$- wherein R^a and R^b are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of R^a and R^b is hydrogen or alkyl and the other of R^a and R^b is aroyl or heteroaroyl, and R^c and R^d are independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aralkyl or heteroaralkyl and, where the ring is cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl, the ring system substituent may also include methylene, oxo and thioxo on carbon atoms thereof

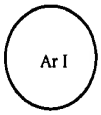
wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein.

2. (Amended) A compound according to claim 1 wherein 

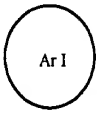
is [optionally substituted aryl,] optionally substituted azaheteroaryl [, or optionally substituted fused arylheterocyclenyl; 

is optionally substituted aryl, optionally substituted heteroaryl, or optionally substituted fused arylheterocyclenyl; and 

is optionally substituted aryl, optionally substituted heteroaryl, optionally substituted fused arylheterocycloalkyl or optionally substituted fused arylheterocyclenyl].

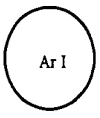
20. (Twice Amended) A compound according to claim 1 wherein 

is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, [*N*-alkyl-quinolin-4-onyl, quinazolin-4-onyl,] benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, [indolinyl] oxazolyl, thiazolyl, oxadiazolyl, isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl [, phenyl, or napthalenyl] group [, wherein the substituent is a ring system substituent].

21. (Amended) A compound according to claim 1 wherein 

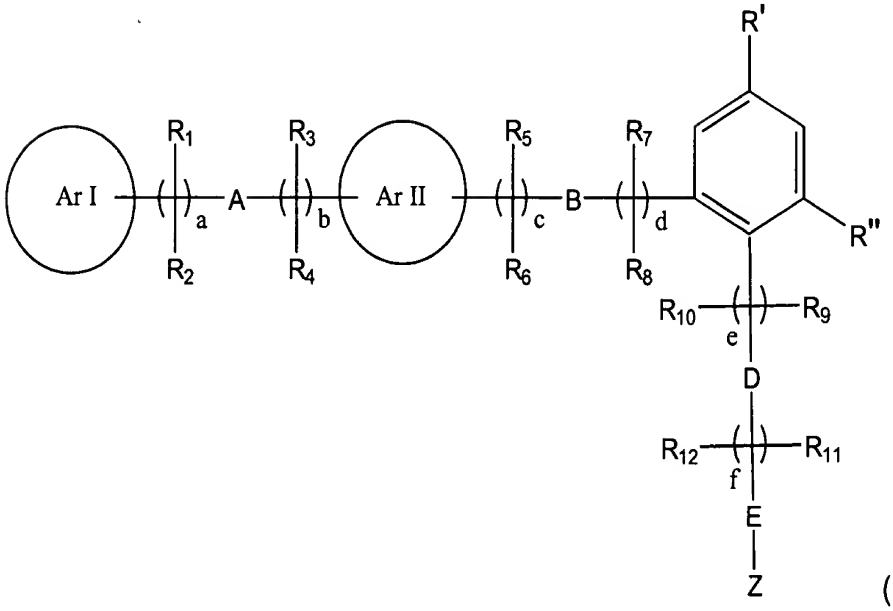
is unsubstituted quinolin-2-yl, 3-substituted quinolin-2-yl, 4-substituted quinolin-2-yl, 6-substituted quinolin-2-yl or 7 substituted quinolin-2-yl; an unsubstituted quinozalin-2-yl, 3-substituted quinozalin-2-yl, 6-substituted quinozalin-2-yl or 3,6-disubstituted quinozalin-2-yl; unsubstituted quinazolin-2-yl, 4-substituted quinazolin-2-yl or 6-substituted quinazolin-2-yl; unsubstituted isoquinolin-3-yl, 6-substituted isoquinolin-3-yl or 7-substituted isoquinolin-3-yl; [3-substituted-quinazolin-4-on-2-yl; *N*-substituted quinolin-4-on-2-yl;] 2-substituted-oxazol-4-yl or 2,5 disubstituted-oxazol-4-yl; 4-substituted oxazol-2-yl or 4,5-disubstituted-oxazol-2-yl; 2-substituted thiazol-4-yl or 2,5-

disubstituted thiazol-4-yl; 4-substituted thiazol-2-yl or 4,5-disubstituted-thiazol-2-yl; 5-substituted-[1,2,4]oxadiazol-3-yl; 3-substituted-[1,2,4] oxadiazol-5-yl; 5-substituted-imidazol-2-yl or 3,5-disubstituted-imidazol-2-yl; 2-substituted-imidazol-5-yl or 2,3-disubstituted-imidazol-5-yl; 3-substituted-isoxazol-5-yl; 5-substituted-isoxazol-3-yl; 5-substituted-[1,2,4] thiadiazol-3-yl; 3-substituted-[1,2,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-oxadiazol-5-yl; 1-substituted-pyrazol-3-yl; 3-substituted-pyrazol-5-yl; 3-substituted-[1,2,4]-triazol-5-yl; 1-substituted-[1,2,4]-triazol-3-yl; 3-substituted pyridin-2-yl, 5-substituted pyridin-2-yl, 6-substituted pyridin-2-yl or 3,5-disubstituted pyridin-2-yl; 3-substituted pyrazin-2-yl, 5-substituted pyrazin-2-yl, 6-substituted pyrazin-2-yl or 3,5 disubstituted-pyrazin-2-yl; 5-substituted pyrimidin-2-yl or 6-substituted-pyrimidin-2-yl; 6-substituted-pyridazin-3-yl or 4,6-disubstituted-pyridazin-3-yl; [unsubstituted napthalen-2-yl, 3-substituted napthalen-2-yl, 4-substituted napthalen-2-yl, 6-substituted napthalen-2-yl or 7 substituted napthalen-2-yl; 2-substituted phenyl, 4-substituted phenyl or 2,4-disubstituted phenyl;] unsubstituted -benzothiazol-2-yl or 5-substituted-benzothiazol-2-yl; unsubstituted benzoxazol-2yl or 5-substituted-benzoxazol-2yl; unsubstituted -benzimidazol-2-yl or 5-substituted-benzimidazol-2-yl; unsubstituted -thiophen-2yl, 3-substituted -thiophen-2yl, 6-substituted -thiophen-2yl or 3,6-disubstituted-thiophen-2yl; unsubstituted -benzofuran-2-y, 3-substituted-benzofuran-2-yl, 6-substituted-benzofuran-2-yl or 3,6-disubstituted-benzofuran-2-yl; 3-substituted-benzofuran-6-yl or 3,7-disubstituted-benzofuran-6-yl [, wherein the substituent is a ring system substituent].

22. (Amended) A compound according to claim 21 wherein 

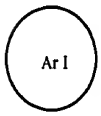
is substituted by a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl [, branched alkyl], fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

27. (Twice Amended) A compound of formula (Ia)

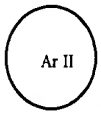


(Ia)

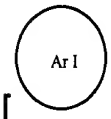
wherein:

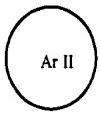


is heteroaryl, which is optionally substituted by one or more ring system substituents;



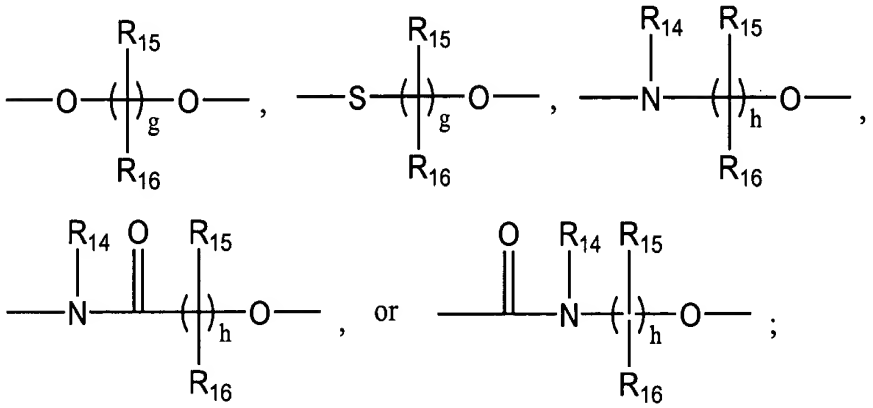
is aryl, which is optionally substituted by one or more ring system substituents;

[

and 

are independently aryl, fused arylcycloalkenyl, fused arylcycloalkyl, fused arylheterocyclenyl, fused arylheterocyclyl, heteroaryl, fused heteroarylcycloalkenyl, fused heteroarylcycloalkyl, fused heteroarylheterocyclenyl, or fused heteroarylheterocyclyl;]

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, [a chemical bond,] ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently -$(CH_2)_q$-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO_2-, -SR_{23}, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$-2,4-thiazolidinedionyl, or tetrazolyl;

R' and R" are, independently, hydrogen or ring system substituents;

R_{21} is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

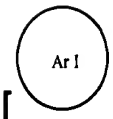
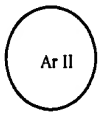
when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

36. (Amended) A compound according to claim 27 wherein:

[ and  are aryl or heteroaryl;]

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen;

R" is methyl [lower alkyl];

Z is $-CO_2H$.

51. (Amended) A method according to claim 50 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides [triclycerides].

58. (Amended) The method according to claim 51, wherein the physiological disorder is a cardiovascular condition.

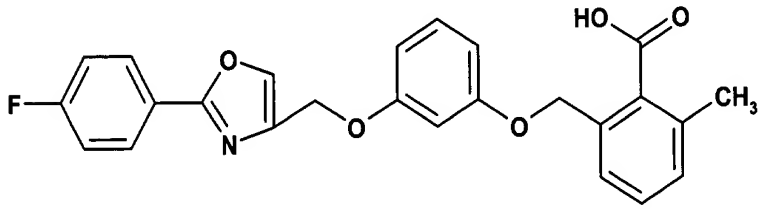
68. (Amended) A method according to claim 67 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides [triclycerides].

75. (Amended) The method according to claim 67, wherein the physiological disorder is a cardiovascular disorder.

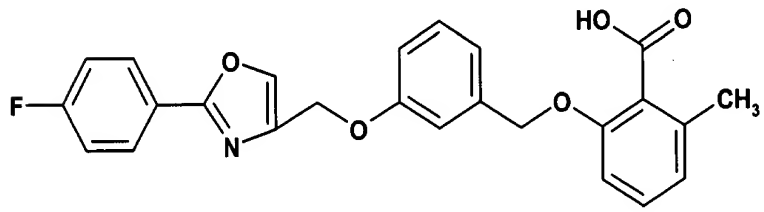
89. (Amended) A compound as claimed in claim 20, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl [, branched alkyl], fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

91. (Amended) A compound as claimed in claim 31 [32], wherein R" is methyl.

94. (Amended) A compound as claimed in claim 1, wherein the compound is



[

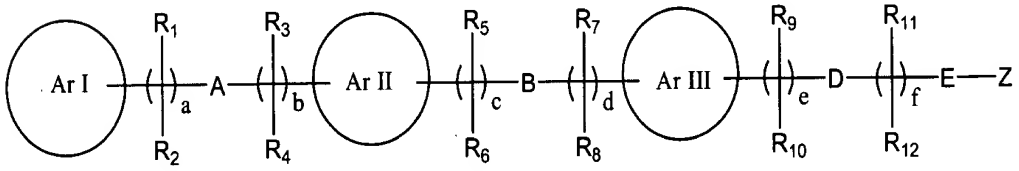


]

or a pharmaceutically acceptable salt, hydrate or solvate thereof.

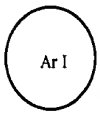
Appendix II with Clean Copy of All Pending Claims, as Amended Herein

1. (Twice Amended) A compound of formula I

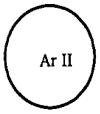


(I)

wherein:



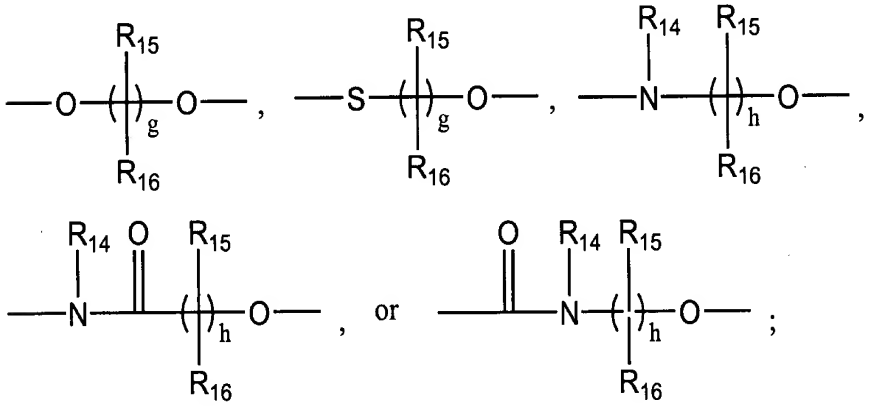
is heteroaryl, which is optionally substituted by one or more ring system substituents;



and

are, independently, aryl, which are optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently $-(CH_2)_q-X$;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO$_2$-, -SR$_{23}$, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$-2,4-thiazolidinedionyl, or tetrazolyl; and

R_{21} is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof;

wherein

"alkyl," when used to designate an alkyl group per se or when used as an alkyl component of any other group, is an aliphatic hydrocarbon group which is straight or branched having 1 to about 20 carbon atoms and is optionally substituted by one or more alkyl group substituents;

"aryl" is an aromatic monocyclic or multicyclic ring system of about 6 to about 14 carbon atoms, which is optionally substituted by one or more ring system substituents;

"heteroaryl" is an aromatic monocyclic or multicyclic ring system of about 5 to about 14 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

"heterocyclyl" is a non-aromatic saturated monocyclic or multicyclic ring system of 3 to about 10 carbon atoms, in which at least one of the carbon atoms in the ring system is replaced by nitrogen, oxygen or sulfur, which is optionally substituted by one or more ring system substituents;

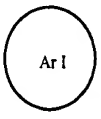
"heteroaralkyl" is a heteroaryl-alkyl group, wherein the heteroaryl and alkyl groups are as defined above;

an "alkyl group substituent" is halo, carboxy, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aryl, alkoxy, alkoxycarbonyl, aralkoxycarbonyl, heteroaralkoxycarbonyl, or Y^1Y^2NCO-, wherein Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or Y^1 and Y^2 taken together with the nitrogen atom to which Y^1 and Y^2 are attached form heterocyclyl

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein.; and

a "ring system substituent" is alkyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aryloxy, aralkoxy, acyl, aroyl, halo, nitro, cyano, carboxy, alkoxycarbonyl, aryloxycarbonyl, aralkoxycarbonyl, alkylsulfonyl, arylsulfonyl, heteroarylsulfonyl, alkylsulfinyl, arylsulfinyl, heteroarylsulfinyl, alkylthio, arylthio, heteroarylthio, aralkylthio, heteroaralkylthio, fused cycloalkyl, fused cycloalkenyl, fused heterocyclyl, fused heterocyclenyl, arylazo, heteroarylazo, R^aR^bN-, R^cR^dNCO-, R^cO_2CN-, or $R^cR^dNSO_2$- wherein R^a and R^b are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of R^a and R^b is hydrogen or alkyl and the other of R^a and R^b is aroyl or heteroaroyl, and R^c and R^d are independently hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, cycloalkenyl, heterocyclyl, heterocyclenyl, aralkyl or heteroaralkyl and, where the ring is cycloalkyl, cycloalkenyl, heterocyclyl or heterocyclenyl, the ring system substituent may also include methylene, oxo and thioxo on carbon atoms thereof

wherein the substituents may contain further alkyl group substituents or ring system substituents as recited herein..

2. (Amended) A compound according to claim 1 wherein 

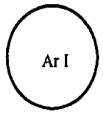
is optionally substituted azaheteroaryl.

7. A compound according to claim 1 wherein a = 1, 2 or 3; R_1 and R_2 are hydrogen; A is -O-; and b = 0.

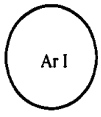
11. A compound according to claim 1 wherein c = 0 or 1; R_5 and R_6 are hydrogen; B is –O-; and d = 0 or 1.

14. A compound according to claim 1 wherein e = 0; f = 0 or 1; D and E is a chemical bond; Z is tetrazolyl, NH_2CO- or $-CO_2R_{21}$; and R_{21} is hydrogen or lower alkyl.

15. A compound according to claim 1 wherein e = 0; f = 0 or 1; D is –O- or a chemical bond; E is a chemical bond; and Z is tetrazolyl, NH_2CO- or $-CO_2R_{21}$; and R_{21} is hydrogen or lower alkyl.

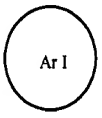
20. (Twice Amended) A compound according to claim 1 wherein 

is an optionally substituted quinolinyl, quinoxalinyl, quinazolinyl, isoquinolinyl, benzoxazolyl, benzimidazolyl, benzothiazolyl, benzofuranyl, benzothiophenyl, oxazolyl, thiazolyl, oxadiazolyl, isoxazolyl, imidazolyl, pyrazol-yl, thiadiazolyl, triazolyl, pyridyl, pyrimidinyl, pyrazinyl, or pyridazinyl group.

21. (Amended) A compound according to claim 1 wherein 

is unsubstituted quinolin-2-yl, 3-substituted quinolin-2-yl, 4-substituted quinolin-2-yl, 6-substituted quinolin-2-yl or 7 substituted quinolin-2-yl; an unsubstituted quinozalin-2-yl, 3-substituted quinozalin-2-yl, 6-substituted quinozalin-2-yl or 3,6-disubstituted quinozalin-2-yl; unsubstituted quinazolin-2-yl, 4-substituted quinazolin-2-yl or 6-substituted quinazolin-2-yl; unsubstituted isoquinolin-3-yl, 6-substituted isoquinolin-3-yl or 7-substituted isoquinolin-3-yl; 2-substituted-oxazol-4-yl or 2,5 disubstituted-oxazol-4-yl; 4-substituted oxazol-2-yl or 4,5-disubstituted-oxazol-2-yl; 2-substituted thiazol-4-yl or 2,5-disubstituted thiazol-4-yl; 4-substituted thiazol-2-yl or 4,5-disubstituted-thiazol-2-yl; 5-substituted-[1,2,4]oxadiazol-3-yl; 3-substituted-[1,2,4] oxadiazol-5-yl; 5-substituted-imidazol-2-yl or 3,5-disubstituted-imidazol-2-yl; 2-substituted-imidazol-5-yl or 2,3-disubstituted-imidazol-5-yl; 3-substituted-isoxazol-5-yl; 5-substituted-isoxazol-3-yl; 5-

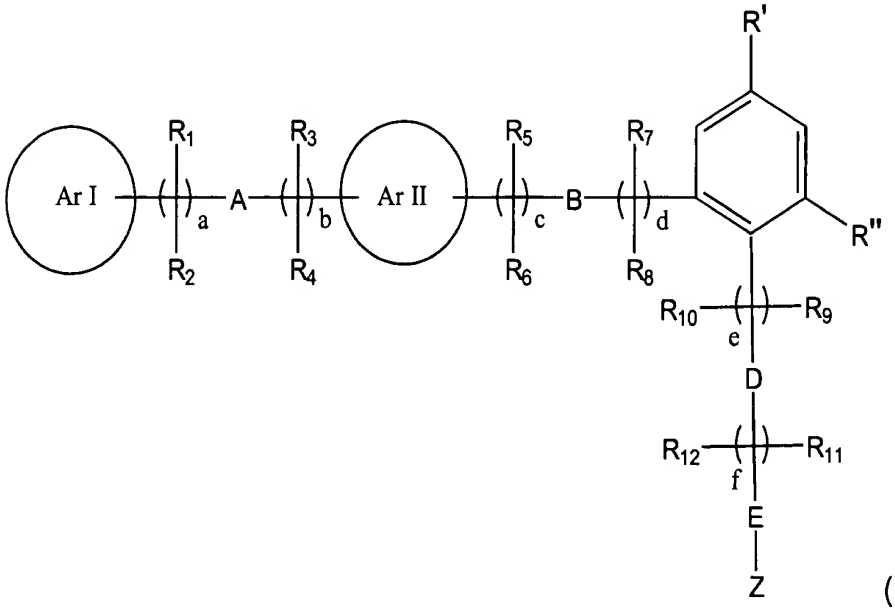
substituted-[1,2,4] thiadiazol-3-yl; 3-substituted-[1,2,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-thiadiazol-5-yl; 2-substituted-[1,3,4]-oxadiazol-5-yl; 1-substituted-pyrazol-3-yl; 3-substituted-pyrazol-5-yl; 3-substituted-[1,2,4]-triazol-5-yl; 1-substituted-[1,2,4]-triazol-3-yl; 3-substituted pyridin-2-yl, 5-substituted pyridin-2-yl, 6-substituted pyridin-2-yl or 3,5-disubstituted pyridin-2-yl; 3-substituted pyrazin-2-yl, 5-substituted pyrazin-2-yl, 6-substituted pyrazin-2-yl or 3,5 disubstituted-pyrazin-2-yl; 5-substituted pyrimidin-2-yl or 6-substituted-pyrimidin-2-yl; 6-substituted-pyridazin-3-yl or 4,6-disubstituted-pyridazin-3-yl; unsubstituted -benzothiazol-2-yl or 5-substituted-benzothiazol-2-yl; unsubstituted benzoxazol-2yl or 5-substituted-benzoxazol-2yl; unsubstituted -benzimidazol-2-yl or 5-substituted-benzimidazol-2-yl; unsubstituted -thiophen-2yl, 3-substituted -thiophen-2yl, 6-substituted -thiophen-2yl or 3,6-disubstituted-thiophen-2yl; unsubstituted -benzofuran-2-y, 3-substituted-benzofuran-2-yl, 6-substituted-benzofuran-2-yl or 3,6-disubstituted-benzofuran-2-yl; 3-substituted-benzofuran-6-yl or 3,7-disubstituted-benzofuran-6-yl.

22. (Amended) A compound according to claim 21 wherein 

is substituted by a substituent selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

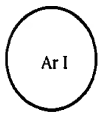
23. A compound according to claim 1 wherein R_1 and R_2 are hydrogen; a = 1; A is –O-; and b = 0.

27. (Twice Amended) A compound of formula (Ia)

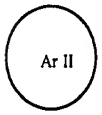


(Ia)

wherein:

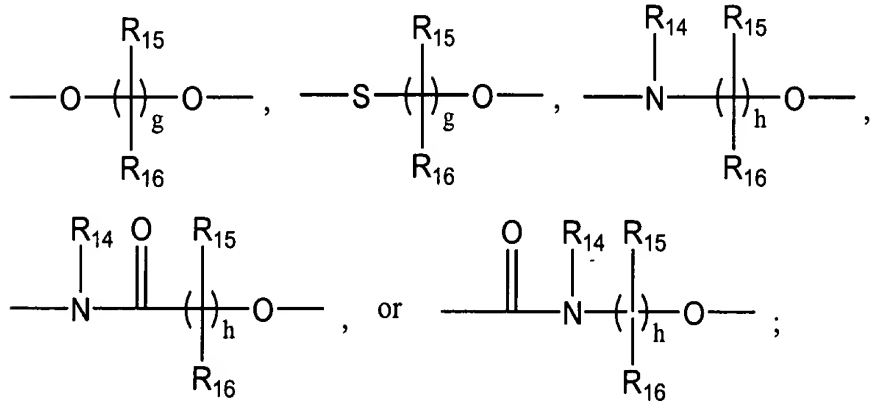


is heteroaryl, which is optionally substituted by one or more ring system substituents;



is aryl, which is optionally substituted by one or more ring system substituents;

A is -O-, -S-, -SO-, -SO_2-, -NR_{13}-, -C(O)-, -$N(R_{14})C(O)$-, -$C(O)N(R_{15})$-, -$N(R_{14})C(O)N(R_{15})$-, -$C(R_{14})$=N-, a chemical bond,



B is –O-, -S-, -SO-, -SO_2-, -NR_{17}-, ethynylene, -C(O)-, -$N(R_{18})C(O)$-, or –$C(O)NR_{18}$-;

D is –O-, -S-, -NR_{19}-, a chemical bond, ethynylene, -$N(R_{20})C(O)$-, -C(O)-, or –$C(O)N(R_{20})$-;

E is a chemical bond or an ethylene group;

a is 0-4;

b is 0-4;

c is 0-4;

d is 0-5;

e is 0-4;

f is 0-6;

g is 1-4;

h is 1-4;

R_1, R_3, R_5, R_7, R_9, and R_{11}, are independently hydrogen, halogen, alkyl, carboxyl, alkoxycarbonyl or aralkyl;

R_2, R_4, R_6, R_8, R_{10} and R_{12}, are independently -$(CH_2)_q$-X;

q is 0-3;

X is hydrogen, halogen, alkyl, alkenyl, cycloalkyl, heterocyclyl, aryl, heteroaryl, aralkyl, heteroaralkyl, hydroxy, alkoxy, aralkoxy, heteroaralkoxy, carboxyl, alkoxycarbonyl, tetrazolyl, acyl, acylHNSO_2-, -SR_{23}, Y^1Y^2N- or Y^3Y^4NCO-;

Y^1 and Y^2 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl, or one of Y^1 and Y^2 is hydrogen or alkyl and the other of Y^1 and Y^2 is acyl or aroyl;

Y^3 and Y^4 are independently hydrogen, alkyl, aryl, aralkyl or heteroaralkyl;

Z is $R_{21}O_2C$-, $R_{21}OC$-, cyclo-imide, -CN, $R_{21}O_2SHNCO$-, $R_{21}O_2SHN$-, $(R_{21})_2NCO$-, $R_{21}O$-2,4-thiazolidinedionyl, or tetrazolyl;

R' and R" are, independently, hydrogen or ring system substituents;

R_{21} is hydrogen, alkyl, aryl, cycloalkyl, or aralkyl;

R_{13}, R_{17}, R_{19} and R_{23} are independently $R_{22}OC$-, $R_{22}NHOC$-, hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl;

R_{14}, R_{15}, R_{16}, R_{18} and R_{20} are independently hydrogen, alkyl, aralkyl, carbonyl, or alkoxycarbonyl;

or R_{14}, and R_{15} taken together with the carbon and nitrogen atoms through which they are linked form a 5 or 6-membered azaheterocyclyl group; or

when a is 2-4, then vicinal R_1 radicals taken together with the carbon atoms to which the R_1 radicals are linked form an ethylene group; or

when b is 2-4, then vicinal R_3 radicals taken together with the carbon atoms to which the R_3 radicals are linked form an ethylene group; or

when c is 2-4, then vicinal R_5 radicals taken together with the carbon atoms to which the R_5 radicals are linked form an ethylene group; or

when d is 2-5, then vicinal R_7 radicals taken together with the carbon atoms to which the R_7 radicals are linked form an ethylene group; or

when e is 2-4, then vicinal R_9 radicals taken together with the carbon atoms to which the R_9 radicals are linked form an ethylene group; or

when f is 2-6, then vicinal R_{11} radicals taken together with the carbon atoms to which the R_{11} radicals are linked form an ethylene group; and

R_{22} is hydrogen, alkyl, aryl, heteroaryl, cycloalkyl, heterocyclyl, heteroaralkyl, or aralkyl; or

a pharmaceutically acceptable salt thereof, an N-oxide thereof, a hydrate thereof or a solvate thereof.

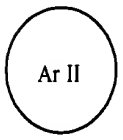
31. (Amended) A compound according to claim 27 wherein

a = 1 or 2;

A is -O-;

b = 0;

R_1, R_2, R_7 and R_8 are independently hydrogen;



is optionally substituted phenyl;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, halo or benzyloxy;

R" is lower alkyl;

Z is $-CO_2H$.

34. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0-1;

B is -O-;

d = 0 or 1, wherein c+d = 1 or 2;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen, aralkoxy, or halo;

R" is lower alkyl;

Z is $-CO_2H$.

35. (Original) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen;

R" is lower alkyl;

Z is $-CO_2H$.

36. (Amended) A compound according to claim 27 wherein:

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

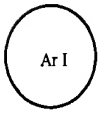
D and E are a chemical bond;

R' is hydrogen;

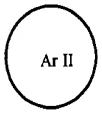
R" is methyl;

Z is $-CO_2H$.

37. (Original) A compound according to claim 27 wherein:



is optionally substituted azaheteroaryl;



is optionally substituted phenyl;

a = 1;

A is -O-;

b = 0;

c = 0;

B is -O-;

d = 1;

e = 0;

f = 0;

D and E are a chemical bond;

R' is hydrogen;

R" is lower alkyl;

Z is CO_2H.

49. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 1 and a pharmaceutically acceptable carrier.

50. A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 1 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, or a pharmaceutically acceptable salt thereof.

51. (Amended) A method according to claim 50 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

52. The method according to claim 51, wherein the physiological disorder is hyperglycemia.

53. The method according to claim 52, wherein the hyperglycemia is diabetes.

54. The method according to claim 52, wherein the hyperglycemia is Type II diabetes.

55. The method according to claim 51, wherein the physiological disorder is hyperinsulinism.

56. The method according to claim 55, wherein the hyperinsulinism is Syndrome X.

57. The method according to claim 51, wherein the physiological disorder is insulin resistance.

58. (Amended) The method according to claim 51, wherein the physiological disorder is a cardiovascular condition.

59. The method according to claim 58, wherein the cardiovascular condition is atherosclerosis.

60. The method according to claim 51, wherein the physiological disorder is hyperlipidemia.

61. The method according to claim 51, wherein the physiological disorder is hypertension.

62. The method according to claim 51, wherein the physiological disorder is an eating disorder.

63. The method according to claim 50 wherein the mediating is agonistic.

64. The method according to claim 50 wherein the mediating is antagonistic.

65. A method for mediating the activity of PPAR-γ receptor comprising contacting said PPAR-γ receptor with a compound of according to claim 1.

66. A pharmaceutical composition comprising a pharmaceutically acceptable amount of the compound according to claim 27 and a pharmaceutically acceptable carrier.

67. A method of treating a patient suffering from a physiological disorder capable of being modulated by a compound according to claim 27 having PPAR ligand binding activity, comprising administering to the patient a pharmaceutically effective amount of the compound, or a pharmaceutically acceptable salt thereof.

68. (Amended) A method according to claim 67 wherein the physiological disorder is associated with a physiological detrimental blood level of insulin, glucose, free fatty acids (FFA), or triglycerides.

69. The method according to claim 67, wherein the physiological disorder is hyperglycemia.

70. The method according to claim 69, wherein the hyperglycemia is diabetes

71. The method according to claim 69, wherein the hyperglycemia is Type II diabetes.

72. The method according to claim 67, wherein the physiological disorder is hyperinsulinism.

73. The method according to claim 72, wherein the hyperinsulinism is Syndrome X.

74. The method according to claim 67, wherein the physiological disorder is insulin resistance.

75. (Amended) The method according to claim 67, wherein the physiological disorder is a cardiovascular disorder.

76. The method according to claim 75, wherein the cardiovascular disorder is atherosclerosis.

77. The method according to claim 67, wherein the physiological disorder is hyperlipidemia.

78. The method according to claim 67, wherein the physiological disorder is hypertension.

79. The method according to claim 67, wherein the physiological disorder is an eating disorder.

80. The method according to claim 67 wherein the mediating is agonistic.

81. The method according to claim 67 wherein the mediating is antagonistic.

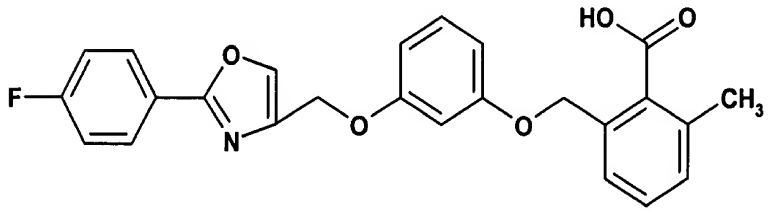
82. A method for mediating the activity of PPAR receptor comprising contacting said PPAR receptor with a compound of according to claim 27.

89. (Amended) A compound as claimed in claim 20, wherein the ring system substituent is selected from the group consisting of phenyl, substituted-phenyl, thienyl, substituted thienyl, cycloalkyl, straight or branched lower alkyl, fluoro, chloro, alkoxy, aralkyloxy, trifluoromethyl and trifluoromethyloxy.

91. (New) A compound as claimed in claim 31, wherein R" is methyl.

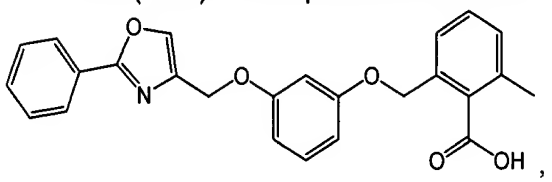
93. (New) A compound as claimed in claim 34, wherein R" is methyl.

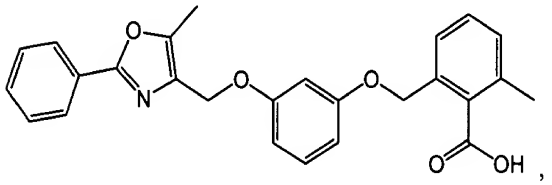
94. (Amended) A compound as claimed in claim 1, wherein the compound is

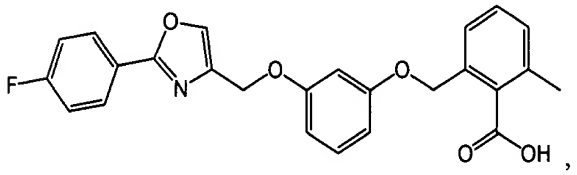


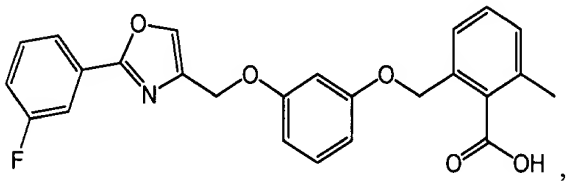
or a pharmaceutically acceptable salt, hydrate or solvate thereof.

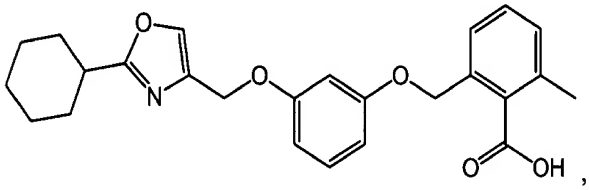
95. (New) A compound as claimed in claim 1, wherein the compound is

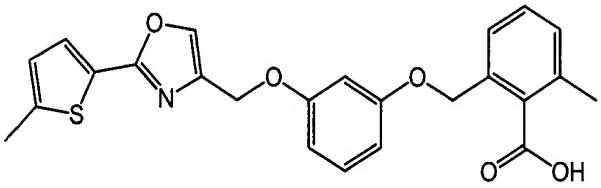




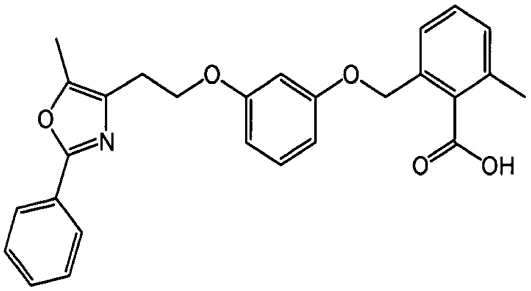






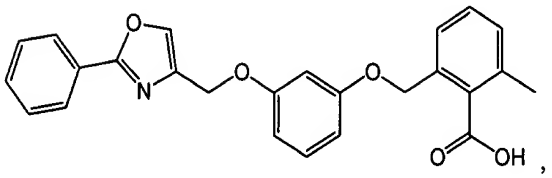


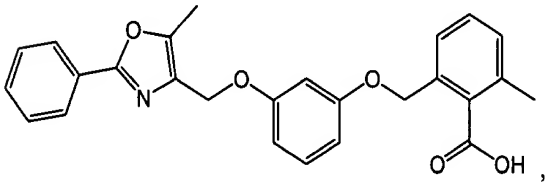
, or

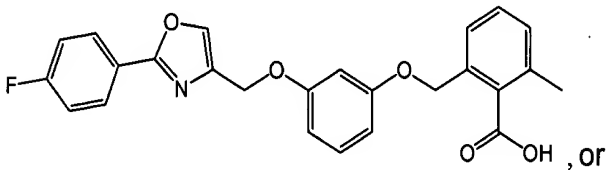


or a pharmaceutically acceptable salt, hydrate or solvate thereof.

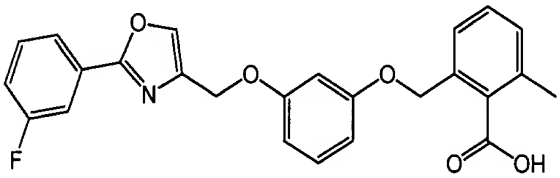
96. (New) A compound as claimed in claim 1, wherein the compound is





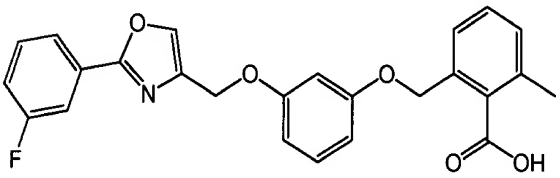


, or

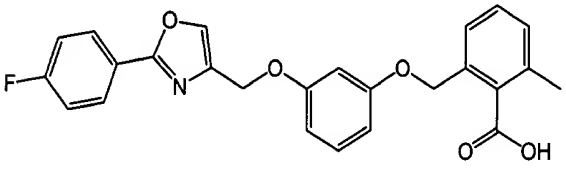


or a pharmaceutically acceptable salt, hydrate or solvate thereof.

97. (New) A compound as claimed in claim 1, wherein the compound is



, or



or a pharmaceutically acceptable salt, hydrate or solvate thereof.